Amendments to the Specification:

In the Sequence Listing, replace the original sequence listing with the amended sequence listing submitted herewith.

At page 24, replace the paragraph beginning at line 1 with the following paragraph.

> By a "DAF-3 polypeptide" is meant a polypeptide that complements (as defined above) a *C. elegans daf-3* mutation and/or that possesses at least 60% amino acid sequence identity to SEQ ID NO: 35, at least 38% amino acid sequence identity to SEQ ID NO: 36, at least 47% amino acid sequence identity to SEQ ID NO: 85, or a combination thereof. Preferably, a DAF-3 polypeptide includes a proline or a glycine at amino acid positions corresponding to *C. elegans daf-3* amino acids at positions 200 (proline) and/or 620 (glycine) in Fig. 12A, respectively, or a combination thereof. For example, the polypeptide may include a proline in the motif GRKGFPHV (SEQ ID NO:~~200~~ 322) or a glycine in the motif RIXXIXXG (where X is any amino acid) (SEQ ID NO:~~201~~ 323).

At page 43, replace the paragraph beginning at line 23 with the following paragraph.

> **Fig. 28** is a graph illustrating the homology of *C. elegans* insulin-like molecules (SEQ ID NOs:117-124) with human insulin (SEQ ID NO:125) and a consensus motif (SEQ ID NO:324).

At page 43, replace the paragraph beginning at line 3 with the following paragraph.

> **Fig. 21A** ~~(SEQ ID NOS:211-215)~~ is an illustration showing that human FKHR (SEQ ID NO:57), FKHRL1 (SEQ ID NO:330), and AFX (SEQ ID NO:331) are the closest relatives to DAF-16 (SEQ ID NO:45). Note that the differentially spliced DAF-15 forkhead domain (DAF-16b) (SEQ ID NO:329) is less homologous.

At page 46, replace the paragraph beginning at line 17 with the following paragraph.

Figs. 39A and 39B illustrate that *daf-19* encodes a homologue of PTEN (MMAC/TEP1). Fig. 39A shows the exon/intron structure of DAF-18 ~~(SEQ ID NO:365-368)~~, including the nucleic acid sequence (SEQ ID NO:327) that encodes amino acids, 570-578 (SEQ ID NO:306) and the nucleic acids (SEQ ID NO:328) that encode amino acids 579-589 (SEQ ID NO:327). The phosphatase domain is indicated in gray. The bottom of this figure indicates that *daf-18(e1375)* has a 30 base pair insertion in the fourth exon. 13 base pairs (shaded) are duplicated along with two smaller segments of the repeat (thick bars). This mutation introduces a premature stop codon (*). Fig. 39B shows an alignment of the phosphatase domains of DAF-18 and PTEN (GeneBank accession U93051) (SEQ ID ~~NO:369-378~~ NOs:308 and 309) Pileup (GCG) was used to align the entire coding sequence. The phosphatase domain is shown with identical amino acids shaded. The probable active site Cys-$(X)_5$-Arg sequence is indicated with a bar.

At page 47, replace the paragraph beginning at line 3 with the following paragraph.

Figs. 40A and 40B show the amino acid and nucleic acid sequences of the *C. elegans daf-18* gene (SEQ ID ~~NO:379-380~~ 310 and 311).

At page 47, replace the paragraph beginning at line 18 with the following paragraph.

Fig. 42 shows the *C. elegans cod-5* nucleic acid and amino acid sequences (SEQ ID ~~NO:381-382~~ NOs: 312 and 313).

At page 47, replace the paragraph beginning at line 20 with the following paragraph.

~~**Figs.**~~ **Fig 43** shows the *C. elegans cod-5* knockout cDNA and amino acid sequences (SEQ ID ~~NO:383-384~~ NOs:314 and 315).

At page 50, replace the paragraph beginning at line 4 with the following

paragraph.

Figs. 47A and 47B show the nucleic acid and amino acid sequences of a human DAF-7 homologue (SEQ ID ~~NO: 385-386~~ NOs: 316 and 317).

At page 95, replace the paragraph beginning at line 9, and spanning page 96, with the following paragraph.

The present model, based on genetic evidence that Akt/PKB couples insulin receptor-like signaling to transcriptional output via the DAF-16 Fork head transcription factor in *C. elegans*, predicts that Akt/PKB will have transcriptional outputs in insulin-like signaling across phylogeny. It was previously suggested that the human homologs of the DAF-16 transcription factor (AFX, FKHR, FKHRL1 and AF6q21) may be the pertinent downsteam effectors of insulin signaling in humans (Ogg et al., *Nature* 389:994-999, 1997). Two of the consensus Akt/PKB sites conserved in DAF-16 and its human homologs are located outside of the Fork head DNA binding domain, and two sites are located in the highly basic W2 region of the Fork head domain that has been shown to mediate DNA phosphate backbone contacts (Clark et al. (1993) Nature 364:412-420). Insulin stimulated Akt/PKB phosphorylation of the W2 sites may affect DNA binding whereas the other conserved sites may affect transactivation. A recent report shows that Akt/PKB mediates insulin dependent repression of the insulin-like growth factor binding protein-1 (IGFBP-1) gene in HepG2 cells via a conserved insulin response sequence (CAAAAC/TAA) (SEQ ID NO:318) (Cichy et al., *J. Biol. Chem.* 273:6482-6487, 1998). Interestingly, we have determined that DAF-16 binds to this same insulin response sequence *in vitro*. We propose that Akt/PKB mediates its transcriptional effects on insulin responsive genes such as IGFBP-1 via the human homologs of DAF-16: AFX, FKHR, FKHRL1, or AF6q21.

At page 121, replace the paragraph beginning at line 2 with the following paragraph.

We have constructed a full length protein fusion of GFP to a highly expressed glucose transporter orthologue in the worm genome: H17B01. The H17B01.1 (GLUT) GFP fusion was amplified with primer CAW59 (ccactatggccgagatttcc) (SEQ ID NO: 319) and CAW60

(ccagtgaaaagttcttctcctttcttcctcttctcgaattcgga) (SEQ ID NO: 320). CAW 59 is the promoter primer and corresponds to nucleotides 31101-31120 in cosmid H17B01 and 39249-39268 in YAC Y51H7.contig253. Primer CAW60 is the GFP-fusion primer. The first 23 nucleotides are GFP and the last 21 are GLUT bottom strand (i.e., cttcctcttctcgaattcggc) (SEQ ID NO:321) corresponding to 48128-48108 in Y51H7.contig253 and 5015-5035 in C13F7 (the cosmid that joins H17B01). The protein sequence is as follows (SEQ ID NO: 208):

At page 214, replace the paragraph beginning at line 1 with the following paragraph.

DAF-7 (9 amino acid motif) (SEQ ID NO:~~364~~ 304).
GWDXXIAPK